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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,936	03/25/2005	Ayrookaran J. Poulose	GC717-2-US	1489

5100 7590 11/20/2006

GENENCOR INTERNATIONAL, INC.
ATTENTION: LEGAL DEPARTMENT
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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/500,936	POULOSE, AYROOKARAN J.	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9,10 and 15-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9,10 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's Response filed 26 September 2006 has been entered, amending the specification and claims, and canceling claims 5-8 and 11-14, thus claims 1-4, 9, 10, and 15-18 remain in the application. These amendments overcome objections of record to the specification and claims stated in the communication mailed 27 March 2006, and amendments to claims 1-4, 9 and 10 resolve several bases for rejections of the claims under 35 U.S.C. § 112, first and second paragraphs, in the communication mailed 27 March 2006. This communication is not made final because new grounds of rejection are stated below in view of the amendments to the specification and dependencies of claims 9 and 10 from claim 1. While the amendment of claim 1 avoids the prior art rejections of record, a new ground of rejection over further prior art is also stated below.

Information Disclosure Statement

A document filed 13 March 2006 indicated that three pages of PTO-Forms 1449 had been filed as part of an Information Disclosure Statement [IDS] but no documents other than a 1-page transmittal letter and a 4-page cover letter were actually submitted. Should Applicant wish that any US Patents, foreign patents, journal publications, or other documentation be considered by the examiner during the course of prosecution of the instant application, a copy of each document, save for US Patents, must both be submitted and cited on a PTO-Form 1449 in an Information Disclosure Statement accompanied either by the appropriate fee, or an authorization to charge any required fees, under 37 C.F.R. §§ 1.16 and 1.17.

Claim Objections

Claim 10 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 4. When two claims in an application are duplicates or else are so close in

content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. Here, the functional limitations of the intervening claim 9 fail to distinguish the structure defined by both of claims 4 and 10. See MPEP § 706.03(k).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 and 15-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 and 18 of copending Application No. 10/498,714. Although the conflicting claims are not identical, they are not patentably distinct from each other because the functional limitations of the modified proteases recited by claims 1-3 herein, and features of the encoding DNAs, expression vectors, host cells, and cleaning compositions of claims 15-18 herein, fail to distinguish the inherently identical structures of modified proteases, encoding DNA,

expression vectors, host cells, and cleaning compositions embraced by the claims 1-8 and 18 of the copending application which describe amino acid substitutions at the subtilisin BPN'-correspondent position 26 in a generic subtilisin. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 3, 9, and 10 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification fails to exemplify or describe an improved wash performance, or an improved stability, either for a generic subtilisin or for a mature subtilisin BPN' – the amino acid sequence of which is set forth in SEQ ID NO:3 – that has an amino acid substitution of either V26T or V26S by comparison with a subtilisin having the amino acid sequence set forth in SEQ ID NO:2, which is the amino acid sequence of the subtilisin BPN' precursor. The specification, however, discloses only an improved thermal stability, and a correspondingly improved wash performance at elevated temperatures, when the CG36 subtilisin having the amino acid sequence set forth in SEQ ID NO:6 is modified by an amino acid substitution of either V26T or V26S. Compare Table 3 at pages 32-33 of the specification, where no modified CG36 subtilisin having amino acid substitutions of either V26T or V26S is shown to meet the limitations of claim 9, with Table 4 at pages 34-36 of the specification, where three modified CG36 subtilisins having amino acid substitutions of either V26T or V26S are shown to have

improved thermal stability and improved wash performance at an elevated temperature, 50°C, for twenty minutes, corresponding to limitations of the amended claim 3 if it were to recite SEQ ID NO:6.

Claims 2, 9 and 10 as amended reach generic subtilases having improved stability and/or wash performance in "hard" water conditions –15 grains per gallon of mixed Ca^{++} and Mg^{++} ion concentration – by comparison with the mature unmodified subtilisin BPN', and claims 2 and 3 as amended reach generic subtilases having improved stability and/or wash performance at elevated wash temperatures by comparison with the mature unmodified subtilisin BPN'. Yet the specification discloses no such comparisons of the stability or wash performance of generic subtilases modified with V26T or V26S with the stability or wash performance of a mature unmodified subtilisin BPN' according to the amended claims 2, 3, 9, and 10. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification discloses no comparison of wash performance in a mixed Ca^{++} and Mg^{++} ion concentration of 15 grains per gallon between a generic modified subtilisin comprising either a V26T or a V26S modification and an unmodified subtilisin BPN' having the amino acid sequence set forth in SEQ ID NO:3 and discloses no more that a comparison of thermal stability between a modified CG36 subtilisin comprising either a V26T or a V26S modification and an unmodified CG36 subtilisin of SEQ ID NO:6. The specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant field of subtilisin modification could not predict the further modifications of generic subtilisins, or further modifications of subtilisin BPN', that must be made to meet limitations of claims 2, 3, 9, and 10 where

the only comparisons of improved characteristics the specification provides are between modified CG36 subtilisins and an unmodified CG36 subtilisin of SEQ ID NO:6.

Claims 2, 3, 9 and 10 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the preparation of modified CG36 subtilisins comprising amino acid substitutions of either V26S or V26T that have improved thermal stability by comparison with an unmodified CG36 subtilisin, does not reasonably provide enablement for the preparation of modified generic subtilisins comprising amino acid substitutions of either valine or threonine at a position corresponding to position 36 in the amino acid sequence of subtilisin BPN' set forth in SEQ ID NO:3 that have improved thermal stability at 50°C for 20 minutes, or improved wash performance in "hard" water conditions, such as a mixed Ca^{++} and Mg^{++} concentration of 15 grains per gallon, by comparison with the stability and/or wash performance of the unmodified subtilisin BPN' set forth in SEQ ID NO:3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 2, 3, 9 and 10 contemplate arbitrary modifications of a generic protease beyond the V26T or V26S modifications of claim 1 to provide a modified, generic, subtilisin having better stability and better wash performance, whether in the conditions recited by claim 9 or thermal stability, by comparison with the wash performance or thermal stability of the unmodified subtilisin BPN'. The specification does not support the introduction of unspecified amino acid alterations in the amino acid sequence of SEQ ID NO:3, or in an amino acid sequence of a generic subtilisin wherein positions are determined by correspondence with the sequence set forth in SEQ ID NO:2, to provide these improved characteristics in a generic subtilase. Indeed, neither the prior art made of record herein nor Applicant's specification can identify amino acid positions further to position 26 in amino acid sequences of generic subtilases that might be altered, nor teach the nature of the alterations that may be made, which permits resulting, modified, subtilases to have improved thermal stability, or improved wash performance in the conditions of claim 9, than the unmodified subtilisin BPN' having the amino acid sequence of SEQ ID NO:3. Mere sequence perturbation cannot enable the design and preparation of nucleotide sequences encoding a myriad of divergent protease enzymes

and provide the public with a modified generic subtilase that meets limitations of claims 2, 3, 9, and 10 as amended on 26 September 2006.

It is well settled that 35 U.S.C. § 112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. § 112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing eight factors relevant to analysis of enablement). Applying the factors discussed in *Wands* to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the amino acid sequences of subtilases other than the CG36 subtilisin having the amino acid sequence set forth in SEQ ID NO:6 to meet the performance characteristics recited in claims 2, 3, 9, and 10,

b) the specification lacks working examples wherein the amino acid sequences of subtilases other than the CG36 subtilisin having the amino acid sequence set forth in SEQ ID NO:6 are modified to meet the performance characteristics recited in claims 2, 3, 9, and 10, and,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such modification of generic subtilases.

Thus the scope of subject matter embraced by the amended claims 2, 3, 9, and 10 is unsupported by the present specification even if taken in combination with teachings available in the prior art. Amendments of claims 2 and 3 to recite comparisons with the unmodified subtilisin CG36 having the amino acid sequence set forth in SEQ ID NO:6, and the cancellation of claim 9, will overcome this rejection.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 9 and 10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 and 9 are indefinite because, if the recitations identifying the amino acid sequence of the unmodified subtilisin BPN' are intended, the wrong sequence identifier is recited at the close of each claim. This is demonstrated by six separate amendments to the specification filed 26 September 2006 identifying the *Bacillus amyloliquefaciens* subtilisin as having the amino acid sequence set forth in SEQ ID NO:3. Amending claims 1-3 and 9 to recite the correct sequence identifier, SEQ ID NO:3, will overcome this aspect of the rejection under the second paragraph of the statute but would not overcome rejections above under the first paragraph of the statute.

Claim 10 is indefinite in depending from claim 9 where it commences by describing positional equivalence but then requires, in its terminal clause, that a protease variant be a "*Bacillus amyloliquefaciens* subtilisin" with the modification N218S. It is not clear what scope is intended for the claim: whether a claimed subtilisin is subtilisin BPN' comprising the N218S substitution as well as either a V26S or a V26T substitution, or a claimed subtilisin is a generic subtilase comprising a N218S substitution at the subtilisin BPN'-correspondent position 218 as well as either a V26S or a V26T substitution at the subtilisin BPN'-correspondent position 26.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 1-4, 9, 10, and 15-18 are rejected under 35 U.S.C. § 102(e) as being anticipated by Estell et al., US 2005/0148159.

Based on a US provisional application filed 31 December 2001 that fully discloses the subject matters of the published application cited herein, Estell et al. disclose a

generic subtilisin comprising either a V26S or a V26T amino acid substitution where this position corresponds to position 26 in the mature *Bacillus amyloliquefaciens* subtilisin and such subtilisins meet the limitations of claims 1-3 and 9 herein because they will inherently possess the properties recited by claims 1-3 and 9 herein. See paragraphs 0053, 0090, and 0127. Estell et al. also disclose generic subtilisins wherein positions are numbered corresponding to the sequence of the mature *Bacillus amyloliquefaciens* subtilisin comprising either a V26S or a V26T and further comprising a stabilizing N218S amino acid substitution, meeting limitations of claims 4 and 10 herein. See paragraph 0250. Estell et al. further disclose DNAs that encode the modified subtilisins, expression vectors comprising the DNAs, host cells transformed the expression vectors, and cleaning compositions comprising the modified subtilisins, meeting limitations of claims 15-18 herein. See paragraphs 0049, 0054, 0059, 0067-0071, and 0076-0084.

Claims 1-4, 9, 10, and 15-18 are rejected under 35 U.S.C. § 102(f) because the claimed invention was made by another who was the first inventor of the claimed subject matter.

As noted above, the priority document of Estell et al., US 2005/0148159 fully discloses the invention described by claims 1-4, 9, 10, and 15-18. The seventeen-page priority document claimed for the present application, US provisional application serial No. 60/350,221 filed 16 January 2002, however fails to disclose the particular protease variants of claims 1, 4, and 10, DNAs encoding same, vectors and host cells comprising such DNAs, or compositions comprising these particular protease variants, and also fails to disclose any particular protease variants that satisfy the limitations of claim 2, 3, or 9. Indeed, pages 5, 13, 14, and 16 of the priority document disclose no subtilisin comprising either a V26S or a V26T, or further comprising a stabilizing N218S amino acid substitution, where the positions are numbered according to the amino acid sequence of the mature *Bacillus amyloliquefaciens* subtilisin, meeting limitations of

claims 4 and 10 herein. Neither are there any Tables provided in the US provisional application serial No. 60/350,221 that disclose any subtilisin comprising either a V26S or a V26T, or further comprising a stabilizing N218S amino acid substitution. Thus the inventive entity of Estell et al., an entity other than the instant Applicant, was clearly the first to invent the claimed subject matter.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
9 November 2006

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER